PATENT COOPERATION TREATY

PCT

REC'D 24 JUN 2005
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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION See Form PCT/IPEA/416	
P06663PC00/HRO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE 2004/000526	02.04.2004	02.04.2003
International Patent Classification (IPC) or national classification and IPC		
C07K 7/08, G01N 33/564		
Applicant		
Pharmacia Diagnostics AB et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 4 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.01.2005	13.06.2005
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Lars Wallentin/ELY Telephone No. +46 8 782 25 00

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE 2004/000526

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☐ the international application as originally filed/furnished

☒ the description:

pages 1-21 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* 22-25 received by this Authority on 03-06-2005
pages* _____ received by this Authority on _____

☒ the drawings:

pages 1-7 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE 2004/000526

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-20	YES
	Claims		NO
Inventive step (IS)	Claims	1-20	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-20	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Cited document:

D1: WO9911667A1

Document D1 is considered to represent the closest prior art. This document relates to a method for producing peptides containing methylated arginines (see the abstract). The methylation is essential for the reaction with antibodies in serum from patients suffering from systemic lupus erythematosus (SLE). Sequence 19 relates to a peptide with 23 amino acids (part of SdD3). Position 112 can advantageously be dimethylated (see page 12, line 20 - page 13, line 3). There are also other peptides of different length, for instance sequences 5 and 6, which are 15 and 16 amino acids long respectively. The peptides can be used in a diagnostic kit (see the claims).

The invention according to claim 1 differs from D1 in that the arginine is symmetrically dimethylated. D1 discloses arginine residues that are preferably dimethylated in an asymmetrical way.

The effect of the difference is according to the applicant that the peptides are capable of detecting a highly specific subpopulation of anti-Sm antibodies which are exclusively present in patients with SLE. In D1 it has not been shown that the peptides described are capable to discriminate between SLE patients and patients suffering from other related and unrelated diseases.

Nothing stated in D1 leads the skilled person to a peptide with symmetrical dimethylated arginine. Therefore the invention according to claim 1 involves an inventive step.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: V

For the same reasons, the use according to claim 5, the kit according to claim 14 and the method according to claim 20 involves an inventive step.

Claims 2-4, 6-13 and 14-19 are dependent on claims 1, 5 and 14 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

The invention according to claims 1-20 is also industrially applicable.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The subject matter of claims 1, 4, 12, 14-16, 19 and 20 is not sufficiently defined. It does not contain the amino acid sequence or position of the dimethylated arginine in combination with sequence name. These features are necessary to solve the technical problem with which the application is concerned (Article 6). It has not been shown in the application that all the peptides in claims 1, 4, 12, 14-16, 19 and 20 have the desired properties. From the wordings of the present claims, the skilled person would therefore not know which of the peptides he would have to select to obtain the desired effect.

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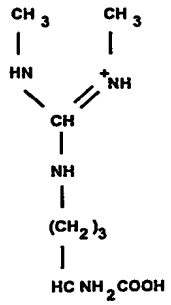
PCT/SE2004/000526
Amended claims 2005-06-01

1) A peptide (S33) containing 15-16 amino acids, comprising symmetrical dimethylated arginine (sDMA), that is able to react with antibodies which are present in sera from patients with systemic lupus erythematosus (SLE) .

2) The S33 peptide according to claim 1 comprising the amino acid sequence
AARGsdRGRGMGRGNIF.

3) A peptide according to claims 1 and 2 where the dimethylated arginine has the position 112 in the polypeptide sequence of SmD3.

4) The peptide according to claims 1 or 2 or 3, wherein the structure of the symmetric dimethylated arginine is



5) Use of a peptide (S33) containing 15-16 amino acids, comprising symmetrical dimethylated arginine (sDMA), that is able to react with antibodies that are present in sera from patients with systemic lupus erythematosus (SLE) for the manufacture of a composition for diagnosis of SLE patients.

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Amended claims 2005-06-01

6) Use according to claim 5, wherein the diagnosis isdifferential diagnosis to distinguish between SLE patients and patients with mixed connective tissue disease (MCTD).

7) Use according to claim 5, wherein the diagnosis is an in vitro diagnosis of SLE .

8) Use according to claim 5, wherein said composition is used for in vitro monitoring of the disease activity of dsDNA negative SLE patients.

9) Use according to claim 5, wherein said composition is used for differentiation between SLE and MCTD.

10) Use according to any of claims 5 to 9, wherein said peptide comprises the amino acid sequence

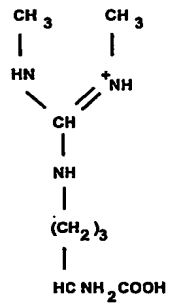
AARGsdRGRGMGRGNIF

11) Use according to any of claims 5 to 10 where the dimethylated arginine has the position 112 in the polypeptide sequence of SmD3.

12) Use of a multimer peptide comprising the peptide of claim 1.

PCT/SE2004/000526
Amended claims 2005-06-01

13) Use according to any of claims 5 to 12, wherein the structure of the symmetric dimethylated arginine is



14) A kit for detection of antibodies, comprising a peptide (S33) of 15-16 amino acids of which one is a symmetrical dimethylated arginine (sDMA), and is able to react with said antibodies that are present in sera from patients with systemic lupus erythematosus (SLE).

15) A kit according to claim 14, wherein said peptide is used for in vitro diagnosis of SLE.

16) A kit according to claim 14, wherein, wherein said peptide is used for differential diagnosis to distinguish between SLE and mixed connective tissue disease (MCTD).

17) A kit according to any of claims 14 to 16, wherein said peptide comprises the amino acid sequence

AARGsdRGRGMGRGNIF.

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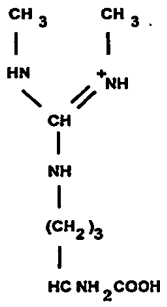
18) A kit for use of a peptide according to any of claims 14 to 17 where the dimethylated arginine has the position 112 in the polypeptide sequence of SmD3.

19) A kit according to any of claims 14 to 18, wherein the structure of the symmetric dimethylated arginine is



20) A method for monitoring a disease activity comprising repeated testing to follow the titer of antibodies able to react with the peptide according to any of claim 1-4 in order to monitor the effect of treatment or the disease activity.